

EXHIBIT 1

Abrogation of tumor necrosis alpha (TNF-alpha) pathway by anti-TNF therapy in hematological malignancies.

Sub-category: Other: Leukemia, Myelodysplasia, and Transplantation

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Abstract:

Background: Tumor necrosis factor-alpha (TNF-alpha) enhances tumor growth and mediates cancer-related inflammatory symptoms by inducing secretion of cytokines. Anti-TNF approaches have been evaluated in pilot studies for cancer treatment and for alleviation of cancer related cachexia, fatigue, and other constitutional symptoms with conflicting results. While the incidence of malignancies with TNF alpha inhibitors (infliximab, adalimumab, etanercept) are not significantly higher than the untreated control population, their role in cancer treatment itself is unclear. We explored the activity and tolerance of TNF-alpha inhibitors in various hematological malignancies. **Methods:** We reviewed the English literature by conducting systematic MEDLINE using the terms TNF-, infliximab, adalimumab, etanercept, cancer therapy, hematologic malignancies, myelodysplastic syndrome (MDS), multiple myeloma (MM), myeloproliferative disease (MPD), chronic lymphocytic leukemia (CLL), and lymphoma from January 2001 to August 2008. We also performed a complete literature search of American Society of Hematology (ASH) and American Society of Clinical Oncology (ASCO) published abstracts. Studies were analyzed for observed activity of TNF alpha inhibitors and also for reported safety. **Results:** Overall 11 phase I and II studies (n = 237; CLL n = 44, MM n = 10, MDS n = 109, MPD n = 51, HCL n = 3, TCL 13, FL 7) that involved anti-TNF- therapy in hematological malignancies were identified. As a single agent, etanercept did not yield significant responses. In conjunction with ATG or azacitidine in low-/intermediate-risk MDS, TNF inhibitors resulted in improvement in cytopenia. Improvement in constitutional symptoms were noted in at least 50% of patients with myelofibrosis(MF)/Ph- MPD. No significant clinical